45. (New) The method of claim 19 wherein at least one of said nucleosides includes a deoxyribose sugar portion

46. (New) The method of claim 19 wherein n is about 5 to about 50.

47. (New) The method of claim 19 wherein n is about 8 to about 30.--

REMARKS

After entry of the proposed amendment, claims 2-15, 17-19 and 20-47 will be pending in this application. Claims 1 and 16 have been canceled. Claims 17, 18 and 19 have been amended without substantive change to be in independent form. Support for new claims 20-47, which claim certain embodiments of the invention, can be found, for example, in the claims as filed.

Applicants submit that the claims presently before the Examiner patentably define the invention over the applied art and are otherwise in condition for ready allowance. An early Office Action to that effect is, therefore, earnestly solicited.

Attached hereto is a marked-up version of the changes made to the specification and claims by the current amendment. The attached page is captioned **"Version with markings to show changes made."**

Respectfully submitted,

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VERSION WITH MARKINGS TO SHOW CHANGES MADE

Claims 1 and 16 have been canceled.

Claims 2-15 and 17-19 have been amended as indicated below:

2. (Once amended) The [compound of claim 1] method of claim 17 wherein L_1 is a Sp phosphorothioate internucleoside linkage and L_2 is a racemic phosphorothioate internucleoside linkage.

3. (Once Amended) The [compound of claim 1] method of claim 17 wherein L_1 and L_2 both are Sp phosphorothioate internucleoside linkages.

4. (Once Amended) The [compound of claim 1] method of claim 17 wherein L_1 is a Rp phosphorothioate internucleoside linkage and L_2 is a racemic phosphorothioate internucleoside linkage.

5. (Once Amended) The [compound of claim 1] method of claim 17 wherein L_1 and L_2 both are Rp phosphorothioate internucleoside linkages.

6. (Once Amended) The [compound of claim 1] method of claim 17 wherein L_1 or L_2 is CH_2-O-NR.

7. (Once Amended) The [compound of claim 1] method of claim 17 wherein L_1 or L_2 is CH_2-NR-O.

8. (Once Amended) The [compound of claim 1] method of claim 17 wherein L_1 and L_2 are both CH_2-O-NR.

9. (Once amended) The [compound of claim 1] method of claim 17 wherein L_1 and L_2 are both CH_2-NR-O.

10. (Once Amended) The [compound of claim 1] method of claim 17 wherein R is alkyl.

11. (Once Amended) The [compound of claim 1] method of claim 17 wherein R is methyl.

12. (Once Amended) The [compound of claim 1] method of claim 17 wherein at least one of said nucleosides includes a ribose sugar portion.

13. (Once Amended) The [compound of claim 1] method of claim 17 wherein at least one of said nucleosides includes a deoxyribose sugar portion

14. (Once Amended) The [compound of claim 1] method of claim 17 wherein n is about 5 to about 50.

15. (Once Amended) The [compound of claim 1] method of claim 17 wherein n is about 8 to about 30.

17. (Once Amended) A method of modulating the production or activity of a protein in an organism, comprising contacting said organism with a compound [of claim 1] comprising a plurality of covalently-bound nucleosides, said compound having the formula:

$$(5')\ N_U\text{-}L_1\text{-}[N_U\text{-}L_S]_n\text{-}N_U\text{-}L_2\text{-}N_U\ (3')$$

wherein:

each N_U is, independently, a nucleoside that includes a ribose or deoxyribose

sugar portion and a base portion;

L_s is a racemic phosphorothioate internucleoside linkage;

n is 1-200; and

L_1 and L_2 are independently selected such that:

L_1 is a Sp phosphorothioate internucleoside linkage, L_2 is a racemic phosphorothioate internucleoside linkage, and said compound has greater than about 60% stereoisomeric purity; or

L_1 and L_2 both are Sp phosphorothioate internucleoside linkages and said compound has greater than about 60% stereoisomeric purity; or

L_1 is a Rp phosphorothioate internucleoside linkage, L_2 is a racemic phosphorothioate internucleoside linkage, and said compound has greater than about 60% stereoisomeric purity; or

L_1 and L_2 both are Rp phosphorothioate internucleoside linkages and said compound has greater than about 60% stereoisomeric purity; or

L_1 and L_2, independently, have the formula CH_2-O-NR or CH_2-NR-O wherein R is H, alkyl having 1 to about 10 carbon atoms, alkenyl having 2 to about 10 carbon atoms, alkynyl having 2 to about 10 carbon atoms; alkaryl having 7 to about 14 carbon atoms, aralkyl having 7 to about 14 carbon atoms.

18. (Once Amended) A method of treating an organism having a disease characterized by the undesired production of a protein, said method comprising contacting said organism with a compound [of claim 1] comprising a plurality of covalently-bound nucleosides,

said compound having the formula:

$$(5')\ N_U\text{-}L_1\text{-}[N_U\text{-}L_S]_n\text{-}N_U\text{-}L_2\text{-}N_U\ (3')$$

wherein:

each N_U is, independently, a nucleoside that includes a ribose or deoxyribose sugar portion and a base portion;

L_s is a racemic phosphorothioate internucleoside linkage;

n is 1-200; and

L_1 and L_2 are independently selected such that:

L_1 is a Sp phosphorothioate internucleoside linkage, L_2 is a racemic phosphorothioate internucleoside linkage, and said compound has greater than about 60% stereoisomeric purity; or

L_1 and L_2 both are Sp phosphorothioate internucleoside linkages and said compound has greater than about 60% stereoisomeric purity; or

L_1 is a Rp phosphorothioate internucleoside linkage, L_2 is a racemic phosphorothioate internucleoside linkage, and said compound has greater than about 60% stereoisomeric purity; or

L_1 and L_2 both are Rp phosphorothioate internucleoside linkages and said compound has greater than about 60% stereoisomeric purity; or

L_1 and L_2, independently, have the formula CH_2-O-NR or CH_2-NR-O wherein R is H, alkyl having 1 to about 10 carbon atoms, alkenyl having 2 to

about 10 carbon atoms, alkynyl having 2 to about 10 carbon atoms; alkaryl having 7 to about 14 carbon atoms, aralkyl having 7 to about 14 carbon atoms.

19. (Once Amended) A method of assaying a nucleic acid, comprising contacting a solution suspected to contain said nucleic acid with a compound [of claim 1] comprising a plurality of covalently-bound nucleosides, said compound having the formula:

$$(5')\ N_U\text{-}L_1\text{-}[N_U\text{-}L_S]_n\text{-}N_U\text{-}L_2\text{-}N_U\ (3')$$

wherein:

each N_U is, independently, a nucleoside that includes a ribose or deoxyribose sugar portion and a base portion;

L_s is a racemic phosphorothioate internucleoside linkage;

n is 1-200; and

L_1 and L_2 are independently selected such that:

L_1 is a Sp phosphorothioate internucleoside linkage, L_2 is a racemic phosphorothioate internucleoside linkage, and said compound has greater than about 60% stereoisomeric purity; or

L_1 and L_2 both are Sp phosphorothioate internucleoside linkages and said compound has greater than about 60% stereoisomeric purity; or

L_1 is a Rp phosphorothioate internucleoside linkage, L_2 is a racemic phosphorothioate internucleoside linkage, and said compound has greater than

about 60% stereoisomeric purity; or

L_1 and L_2 both are Rp phosphorothioate internucleoside linkages and said compound has greater than about 60% stereoisomeric purity; or

L_1 and L_2, independently, have the formula CH_2-O-NR or CH_2-NR-O wherein R is H, alkyl having 1 to about 10 carbon atoms, alkenyl having 2 to about 10 carbon atoms, alkynyl having 2 to about 10 carbon atoms; alkaryl having 7 to about 14 carbon atoms, aralkyl having 7 to about 14 carbon atoms.

New claims 20-47 have been added.